DETAILED ACTION

Application Status

Claims 1-168 are currently pending.

In response to a previous Office action, a non-final action (mailed on November 29, 2010), Applicants filed a response and amendment on May 26, 2011, amending claims 1-3, 5-7, 91, 118, 125, 134-135, 147 and 157, and adding new claims 167-168 that is acknowledged. Claims 8-90, 92-116, 117, 121-124, 126-133, 136-146, 149-154, 159-163 and 164 remain withdrawn as being drawn to a nonelected invention.

Claims 1-7, 91, 118-120, 125, 134-135, 147-148, 155-158, 165-166 and 167-168 are under consideration and are present for examination.

Applicants' arguments filed on May 26, 2011, have been fully considered and are deemed persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Non-compliance of Sequence Rule

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that Claim 91 recites the amino acid sequence of motif of "GDSL-GRTT, GDSL-ARTT, GDSN-GRTT, GDSN-ARTT and SDSL-GRTT" without a corresponding sequence identifier. See particularly 37 CFR 1.821(d).

Withdrawn-Claim Rejections - 35 USC § 112

The previous rejection of claims 1-2, 3, 5-7, 118, 134-135, 147-148, 155-158, 165 and 166 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicants amendment of claims and persuasive arguments.

The previous rejection of claims 1-2, 3, 5-7, 118, 134-135, 147-148, 155-158, 165 and 166 under 35 U.S.C. 112, first paragraph on Scope of enablement is withdrawn in view of applicants amendment of claims and persuasive arguments.

New - Claim Rejections - 35 U.S.C. § 112

Claims 1-2, 3, 5-7, 91, 118, 125, 134-135, 147-148, 155-158, 165-167 and 168 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to any isolated perhydrolase enzyme from any source having few motifs such as GDSL-GRTT, GDSL-ARTT, GDSN-GRTT, GDSN-ARTT and SDSL-GRTT (claim 91) or any M. smegmatis species, which is at least 70-90% homologous to SEQ ID NO: 2 of M. smegmatis perhydrolase (claims 1-2, 3, 5-7, 118, 134-135, 147-148, 155-158, 165-167 and 168) or encoded by any portion of SEQ ID NO: 1 (claim 125). The specification discloses the reduction of practice of several species of variants of M. smegmatis perhydrolase of SEQ ID NO: 2 having perhydrolase activity. There is no other drawing or structural formula disclosed of a perhydrolase polypeptides having 70-90% sequence homologous to perhydrolase polypeptide of

SEQ ID NO: 2 from M. smegmatis and having perhydrolase activity. The specification does not contain any disclosure of any variants of M. smegmatis perhydrolase, which is 70-90% homologous to M. smegmatis perhydrolase of SEQ ID NO: 2 combined with pre-existing knowledge in the art regarding the genetic code and its redundancies would have put one in possession of the genus. With the aid of computer, one of skill in the art could identify all of the polypeptides with at least 70-90% sequence homologous to M. smegmatis perhydrolase of SEQ ID NO: 2. However, there is no teaching regarding which 70-90% of the amino acids can vary from SEQ ID NO: 2 and still result in a protein that retains perhydrolase activity. Furthermore, there is no disclosed or art-recognized correlation between any structures other than SEQ ID NO: 2 and having perhydrolase activity. While general knowledge in the art may have allowed one of skill in the art to identify other proteins expected to have the same or similar tertiary structure, in this example there is no general knowledge in the art about perhydrolase activity to suggest that general similarity of structure confers the activity. Accordingly, one of skill in the art would accept the disclosure of SEQ ID NO: 2 as representative of other proteins having perhydrolase activity. The specification, taken with the pre-existing knowledge in the art of amino acid substitution and the genetic code, fails to satisfy the written description requirement under 35 USC 112, first paragraph.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-2, 3, 5-7, 91, 118, 125, 134-135, 147-148, 155-158, 165-167 and 168 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a perhydrolase enzyme polypeptide of SEQ ID NO: 2 from M. smegmatis and several variants of

SEQ ID NO: 2, which is encoded by SEQ ID NO: 1, does not reasonably provide enablement for any perhydrolase enzyme from any source having any structure having few motifs such as GDSL-GRTT, GDSL-ARTT, GDSN-GRTT, GDSN-ARTT and SDSL-GRTT (claim 91) or from ant M. smegmatis species, which is at least 70-90% homologous to M. smegmatis perhydrolase of SEQ ID NO: 2 (claims 1-2, 3, 5-7, 118, 134-135, 147-148, 155-158, 165-167 and 168) or encoded by any portion of SEQ ID NO: 1 (claim 125). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in In re Wands (858 F.2d 731,737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows:

(1) quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence and absence of working examples, (4) the nature of the invention, (5) the state of prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The factors, which have, lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed below:

The breadth of the claims:

Claims 1-2, 3, 5-7, 91, 118, 125, 134-135, 147-148, 155-158, 165-167 and 168 are so broad as to encompass any perhydrolase enzyme from any source having any structure having few motifs such as GDSL-GRTT, GDSL-ARTT, GDSN-GRTT, GDSN-ARTT and SDSL-GRTT (claim 91) or from ant M. smegmatis species, which is at least 70-90% homologous to M. smegmatis perhydrolase of SEQ ID NO: 2 (claims 1-2, 3, 5-7, 118, 134-135, 147-148, 155-158,

165-167 and 168) or encoded by any portion of SEQ ID NO: 1 (claim 125). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins including many mutants, variants and recombinants broadly encompassed by the claims. In the instant case the disclosure is limited to the nucleotide and encoded amino acid sequence of only a single protein of SEQ ID NO: 2 isolated from M. smegmatis and several variants of SEQ ID NO: 2.

The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art:

The amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In the instant case, the protein which is 70-90% homologous to any perhydrolase protein of M. smegmatis, i.e. 10-30% comprises many mutants, variants and recombinants. The art clearly teaches the high level of unpredictability with regard to the effect of structural changes in a protein's activity when no guidance/knowledge as to which amino acids are required for activity has been provided. While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. Whisstock et al. (2003, see PTO892) teach that prediction of

protein function from sequence and structure is a difficult problem because homologous proteins often have different functions (see abstract). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. Similarly, at the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. Similarly, Chica et al. (Curr Opin Biotechnol. 2005 Aug;16(4):378-84; PTO 892) teach that the complexity of the structure/function relationship in enzymes has proven to be a factor in limiting the general application of rational enzyme modification and design, where rational enzyme modification and design requires in-depth understanding of structure/function relationships. The teachings of Whisstock et al. and Chica et al. are further supported by the teachings of Witkowski et al. (1999, see PTO892), where it is shown that even small amino acid changes result in enzymatic activity changes.

The amount of direction or guidance presented and the existence of working examples:

The specification discloses a perhydrolase enzyme polypeptide of SEQ ID NO: 2 from M. smegmatis and several variants of SEQ ID NO: 2. However, the specification fails to provide any clue as to the structural elements required in any perhydrolase protein from any source having few motifs or any M. smegmatis species, which is 70-90% homologous to a perhydrolase protein from M. smegmatis of SEQ ID NO: 2, i.e. 10-30% non-homologous to M. smegmatis perhydrolase protein known in the art that are essential for any protein to display perhydrolase enzymatic activity. No correlation between structure and function has been presented.

The specification does not support the broad scope of the claims which encompass any perhydrolase enzyme from any source having any structure having few motifs such as GDSL-GRTT, GDSL-ARTT, GDSN-GRTT, GDSN-ARTT and SDSL-GRTT (claim 91) or from ant M. smegmatis species, which is at least 70-90% homologous to M. smegmatis perhydrolase of SEQ ID NO: 2 (claims 1-2, 3, 5-7, 118, 134-135, 147-148, 155-158, 165-167 and 168) or encoded by any portion of SEQ ID NO: 1 (claim 125) because the specification does **not** establish: (A) regions of the protein structure which may be modified without affecting perhydrolase enzymatic activity and; (B) the general tolerance of perhydrolase polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any perhydrolase polypeptide amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

The quantity of experimentation required practicing the claimed invention based on the teachings of the specification:

While methods of generating or isolating variants of a polynucleotide were well known in the art at the time of invention, it is not routine in the art to screen by trial and error process for (1) all or any protein which is 70-90% homologous to perhydrolase protein of SEQ ID NO: 2 from M. smegmatis, (2) an essentially infinite number of mutants, variants and recombinants of any perhydrolase protein from M. smegmatis. The amino acids modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple point mutations or substitutions. In addition, one skilled in

the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any perhydrolase enzyme from any source having any structure having few motifs such as GDSL-GRTT, GDSL-ARTT, GDSN-GRTT, GDSN-ARTT and SDSL-GRTT (claim 91) or from ant M. smegmatis species, which is at least 70-90% homologous to M. smegmatis perhydrolase of SEQ ID NO: 2 (claims 1-2, 3, 5-7, 118, 134-135, 147-148, 155-158, 165-167 and 168) or encoded by any portion of SEQ ID NO: 1 (claim 125). The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any perhydrolase protein having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Withdrawn-Claim Rejections - 35 USC § 112

The previous rejection of claims 1-2, 3, 5-7, 118, 134-135, 147-148, 155-158, 165 and 166 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of applicants amendment of claims and persuasive arguments.

Withdrawn-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The previous rejection of claims 1, 2, 118, 134-135, 147, 148, 157 and 158 under 35 U.S.C. 102(b) as being anticipated by Poulose et al. (Enzymatic peracid bleaching system with modified enzyme, US 5,108,457, issued on 4/28/1992, see IDS) is withdrawn in view of applicants amendment of claims and persuasive arguments.

Withdrawn-Claim Rejections - 35 USC § 103

The previous rejection of claim 3 under 35 U.S.C. 103(a) as being unpatentable over Poulose et al. (Enzymatic peracid bleaching system with modified enzyme, US 5,108,457, issued on 4/28/1992, see IDS) as applied to claims 1, 2, 118, 134-135, 147, 148, 157 and 158 above and further in view of UniProt Accession No. Q92XZ6, created 12/1/2001) is withdrawn in view of applicant's amendment of claims and persuasive arguments.

Conclusion

Claims 1-2, 3, 5-7, 91, 118, 125, 134-135, 147-148, 155-158, 165-167 and 168 are rejected.

Claim 4 stands allowed.

Claims 119 and 120 are objected to for depending on rejected base but would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 1st and 2nd paragraph, set forth in this Office action.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-273-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free)?

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August 11, 2011